

Atty Dkt. No.: 10990631-2
USSN: 09/900,294

REMARKS

In view of the above amendments and the following remarks, the Examiner is respectfully requested to withdraw the rejections and allow Claims 51-67 and 72-78.

Claim 51 has been amended to specify a step of mixing the sample fluid by moving a bubble within the hybridization chamber to displace the sample fluid. Support for this amendment may be found throughout the specification, e.g., at page 7, lines 18-23; page 8, lines 11-17; page 15, lines 18-24; page 16, lines 15-18; and page 19, lines 9-20. Claim 51 has also been amended to delete the phrase that the surfactant is a polymeric nonionic surfactant which is polyethylene oxide, which phrase is now represented as Claims 60-62.

Claims 56 and 57 have been amended to delete the amendments added in the previous communication, such that these claims are as originally presented.

Claims 60-62, originally presented with the application and cancelled in the previous communication, have been reinstated as original claims 60-62.

Claims 69-71 have been cancelled and rewritten as Claims 72-74. The Applicants note that cancelled claims 69-71, which were added as new in the Applicant's previous communication, were numbered incorrectly and should have been numbered as previously presented Claims 72-74 and not Claims 69-71. Accordingly, such has been addressed herein. The Applicants apologize for any inconvenience or confusion this may have caused.

Claims 75-77 have been added as new. Support for these claims may be found in the specification and the originally filed claims, e.g., at page 13, lines 22-26 and page 13, paragraph bridging page 14, and page 14, second paragraph.

Claim 78 has been added as new and specifies that the cover of Claim 51 has a peripheral lip. Support for this amendment may be found in the specification, e.g., at page 7, line 6; page 12, line 16; page 13, lines 12-26.

The specification has been amended to delete the embedded Internet address. Reference to the company name, Sigma-Aldrich, Co., has been added. The paragraph has been further amended to conform with the deletion of the Internet address.

The title has been amended to describe the claimed invention.

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The specification has been amended to reflect the current status of U.S. patent applications cited therein.

As no new matter has been added by the above amendments, the Applicants respectfully request the entry thereof.

REJECTION UNDER 35 U.S.C. §112, FIRST PARAGRAPH

Claims 51-59, 63-67 and 69-71 have been rejected under 35 U.S.C. §112, first paragraph, as failing to comply with the written description requirement. As noted above, Claims 69-71 have been canceled and re-written as Claims 72-74. As such, this rejection is addressed with respect to Claims 51-59, 63-67 and 72-74.

In making this rejection, the Examiner asserts that the specification lacks an adequate written description to support the breadth of scope for (1) the concentration of polymeric nonionic surfactant, and (2) the dimensions of the device. The Applicants respectfully submit that the specification provides adequate written description for the claimed scope of the surfactant and device dimensions. Of note is that the rejected claims represent originally filed claims (claims amended, e.g., Claim 51, include matter presented in the originally filed claims). As noted in the MPEP at section 2163.03 (emphasis added), "While a question as to whether a specification provides an adequate written description may arise in the context of an original claim which is not described sufficiently (see, e.g., *Regents of the University of California v. Eli Lilly*, 119 F.3d 1559, 43 USPQ2d 1398 (Fed. Cir. 1997)), there is a strong presumption that an adequate written description of the claimed invention is present in the specification as filed... Consequently, rejection of an original claim for lack of written description should be rare."

The Applicants point to the originally filed claims which provide evidence that the Applicants were in possession of the claimed invention at the time the application was filed. As noted in the MPEP section 608.01(I), "[i]n establishing a disclosure, applicant may rely not only on the description and drawing as filed but also on the original claims if their content justifies it."

For example, originally filed Claim 51 recites (emphasis added):

51. A method for conducting a hybridization assay within an enclosed hybridization chamber, comprising:

(a) providing a device comprised of a (i) a substrate having a surface with at least a portion of said surface representing a hybridization region, wherein a plurality of oligonucleotide probes are bound to the substrate surface within the hybridization region and arranged in a spatially defined and physically addressable manner, and (ii) a cover

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which sealingly contacts the substrate surface about the hybridization region, wherein the cover and the hybridization region form an enclosure having an interior space comprising a hybridization chamber; and

(b) introducing into the hybridization chamber a sample fluid comprising (i) a target molecule which may hybridize to a surface-bound molecular probe within the hybridization region, (ii) a hybridization buffer, and (iii) a surfactant of a type and present at a concentration effective to substantially reduce nonspecific binding and promote mixing of components within the sample fluid; and

(c) maintaining hybridization conditions within the hybridization chamber for a period of time sufficient to allow hybridization between the target molecule and a surface-bound molecular probe to occur.

Accordingly, the originally filed claims provide an adequate written description that supports the breadth of scope of the claims as they pertain to the concentration of polymeric nonionic surfactant and to the dimensions of the device.

Furthermore, the Applicants direct the Examiner's attention to the Summary of the Invention section of the application that also provides an adequate written description that supports the breadth of scope of the claims as they pertain to the concentration of polymeric nonionic surfactant and to the dimensions of the device. For example, the specification teaches (emphasis added):

In a first embodiment, an apparatus is provided for use in conducting a chemical or biochemical reaction on a solid surface within an enclosed chamber, wherein the apparatus comprises:

a substrate having a substantially planar surface with at least a portion of the surface representing a reaction area on which chemical or biochemical reactions are conducted;

a plastic cover having a peripheral lip which sealingly contacts the substrate surface about the reaction area, wherein the cover and the reaction area form an enclosure having an interior space comprising a reaction chamber;

a fastening means for immobilizing the cover on the substrate surface and providing a temporary, watertight seal between the cover and the reaction area; and

a means for introducing fluid into the reaction chamber.

In a related embodiment, a method is provided for conducting a hybridization assay within an enclosed hybridization chamber, wherein the method involves:

(a) providing a device comprised of a (i) a substrate having a surface with at least a portion of said surface representing a hybridization

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region, wherein a plurality of molecular probes are bound to the substrate surface within the hybridization region and arranged in a spatially defined and physically addressable manner, and (ii) a cover which sealingly contacts the substrate surface about the hybridization region, wherein the cover and the hybridization region form an enclosure having an interior space comprising a hybridization chamber;

(b) introducing into the hybridization chamber a sample fluid comprising (i) a target molecule which may hybridize to a surface-bound molecular probe within the hybridization region, (ii) a hybridization buffer, and (iii) a surfactant of a type and present at a concentration effective to substantially reduce nonspecific binding and promote mixing of components within the sample fluid; and

(c) maintaining hybridization conditions within the hybridization chamber for a period of time sufficient to allow hybridization between the target molecule and a surface-bound molecular probe to occur.

Accordingly, the specification provides an adequate written description that supports the breadth of scope of the claims as they pertain to the concentration of polymeric nonionic surfactant and to the dimensions of the device.

The Examiner points to particular passages in the application relating to exemplary surfactant concentrations (page 15) and device dimensions (page 13) and concludes that such passages limit the surfactant concentrations and device dimensions that may be claimed to those that are taught in the specific passages of pages 13 and 15. However, as described above, the specification clearly provides support for embodiments that are not so limited (see for example the originally filed claims and the Summary of the Invention). For example, as noted above, the specification teaches a surfactant is present at a concentration effective to substantially reduce nonspecific binding and promote mixing of components within the sample fluid. Furthermore, the passages cited by the Examiner describe exemplary embodiments of the subject invention. For example, in regards to the passage describing exemplary surfactant concentrations, the passage states "The surfactant generally represents between about..." In fact, the cited passage explicitly teaches that "it should be emphasized that the exact concentration will vary with the surfactant selected, and those skilled in the art may readily optimize concentration with respect to the desired result." The Examiner underlined the sentence "'An exemplary sample fluid will contain between about 0.1 wt.% and about 1 wt.% of polyethylene oxide..." However, this sentence explicitly states that such is an exemplary fluid sample.

Likewise with respect to the dimensions of the device, as described above the specification clearly provides support for embodiments that are not limited to the exemplary dimensions taught on

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page 13, for example the originally filed claims and the Summary of the Invention. Furthermore, the passages cited by the Examiner describe exemplary embodiments of the subject invention. For example, the passage cited by the Examiner states that "This chamber height may range from...", indicating that the height merely may have such ranges, but may not.

Accordingly, for at least the reasons described above, the Applicants respectfully submit that the claims are adequately supported by the original disclosure and that the disclosure reasonably suggests that the Applicants were in possession of the claimed invention at the time of filing. As such, the Applicants respectfully request this rejection be withdrawn.

REJECTION UNDER 35 U.S.C. §103

Claims 51-59, 63-65, 66-67 and 69-71 have been rejected under 35 U.S.C. § 103(a) as being unpatentable over Schnipelsky et al., or Zander et al, in view of Wilding et al and Livak et al. As noted above, Claims 69-71 have been canceled and re-written as Claims 72-74. As such, this rejection is addressed with respect to Claims 51-59, 63-65, 66-67 and 72-74.

The M.P.E.P. provides clear guidance on the requirements of a *prima facie* case of obviousness:

To establish a *prima facie* case of obviousness, three basic criteria must be met. First, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. Second, there must be a reasonable expectation of success. Finally, the prior art reference (or references when combined) must teach or suggest all the claim limitations."

M.P.E.P. § 2142. (Emphasis added.)

Thus, the cited reference must teach or suggest all of the limitations of the claimed invention for the claimed invention to be rendered obvious over the reference. As described above, independent Claim 51, and the claims that have depend therefrom, specify that the claimed method includes a step of mixing the sample fluid by moving a bubble within the hybridization chamber to displace the sample fluid. Accordingly, in order to render obvious the subject claims, the cited reference alone or in combination must teach or suggest such a step for mixing a fluid in a hybridization chamber. However, neither of the references teaches or even suggests such a method.

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The primary references relied on by the Examiner in making this rejection (Schnipelsky et al. and Zander et al.) do not teach or suggest a step of mixing a sample fluid in a hybridization chamber by moving a bubble within the hybridization chamber to displace the sample fluid. For example, Schnipelsky et al. teach a cuvette 10, formed by thin sheets 12 and 14 mated together with pockets and connecting passageways. Zander et al. teach an analogous structure. However, neither of these references teaches or even suggests a bubble in a hybridization chamber, let alone mixing chamber contents by moving a bubble in a chamber to displace fluidic contents. In fact, the only reference to mixing of any kind in Schnipelsky et al is found at col. 7, lines 31-34 related to a general discussion of DNA detection. This passage merely states that a cuvette containing all the material for detection and the DNA can be agitated or shaken to promote mixing, but fails to teach or suggest mixing fluid with a bubble to displace the fluid, let alone doing so in a device as claimed. The only other reference to mixing is found at col. 16, lines 34-36 which merely states that "Mixing can be achieved by agitating the entire cuvette, by any conventional means." As such, mixing using a bubble is not taught or suggested in this passage either.

Zander et al. is directed to automatic sealing closure means for closing off a passage in a flexible cuvette and does not even mention mixing of any kind, let alone mixing a fluid using a bubble as claimed in the subject claims.

The other two references (Livak et al. and Wilding et al.) fail to make up for the deficiencies of the primary references. For example, neither Livak et al. nor Wilding et al. teaches or suggests mixing as claimed in the subject claims, i.e., mixing a fluid in a hybridization chamber by moving a bubble to displace the fluid. For example, Wilding et al. is cited solely for disclosing device dimensions and teaches a sample preparation device. However, not only is the sample preparation device of Wilding et al. wholly different than the device as claimed in the subject claims, but Wilding et al. does not teach or even suggest a chamber having a bubble therein and mixing a fluid with the bubble by fluid displacement. In fact, Wilding et al. do not even mention the presence of a bubble in a chamber, let alone moving a bubble to accomplish mixing of a fluid by fluid displacement by a bubble. Livak et al. is cited solely for disclosing a hybridization buffer that includes TRITON-X-100. Specifically, Livak et al. teach oligonucleotide probes for use in a hybridization assay which may be present on a solid support. However, Livak et al do not teach or suggest the device as claimed in the subject claims, nor the step of mixing as claimed.

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Accordingly, for at least the reason that the cited references alone or in combination fail to teach or suggest mixing a sample fluid in a hybridization chamber by moving a bubble within the hybridization chamber to displace the sample fluid, the cited references fail to render obvious the subject claims.

Furthermore, as noted above, the subject claims specify a device that includes a substrate having a surface with at least a portion of the surface having a hybridization region wherein a plurality of probes are bound to the substrate surface within the hybridization region. The claims also specify that the cover sealingly contacts this substrate surface. In other words, in the device as claimed, the cover sealingly contacts the surface of the substrate that has the probes thereon to provide a hybridization chamber. However, no such configuration is taught or otherwise indicated in the cited references. For example, in regards to the detection compartment 40 of the cited references, it is taught that the compartment is formed by the mating of the two thin sheets together. As can be seen for example in Fig. 3 of Schnipelsky et al., the probes are attached to piles 43', 43'' and 43''' which in turn are positioned on a supporting sheet 41. It is taught that "if the oligo capture method is being used, then each pile comprises beads to which are immovably attached the detection probes noted above, constructed to hybridize with the DNA to be detected." That is, neither of the thin sheets, or any other structure for that matter, sealingly contacts a surface of a substrate that has the probes thereon, whether the surface is characterized as the supporting sheet 41 or the beads. In fact, if beads are employed as the probe substrate, a sealing relationship would not result from contact of one of the thin sheets to one or more beads due to the configuration of the beads. Accordingly, for at least this reason, the cited references do not render obvious the subject invention.

Accordingly, for at least the reasons described above, the cited references, alone or in combination, do not render the subject claims obvious. As such, the Applicants respectfully request that this rejection be withdrawn.

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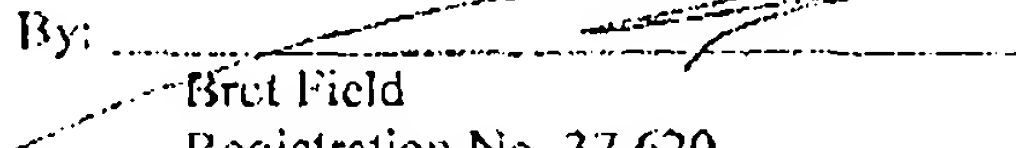
CONCLUSION

In view of the remarks, this application is considered to be in good and proper form for allowance and the Examiner is respectfully requested to pass this application to issue.

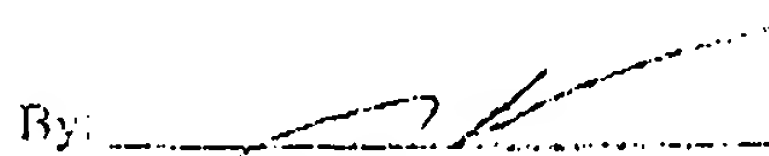
The Commissioner is hereby authorized to charge any fees under 37 C.F.R. §§1.16 and 1.17 which may be required by this paper, or to credit any overpayment, to Deposit Account No. 50-0815, reference no. 10990631-2.

Respectfully submitted,
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